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| 10/540,367 | 06/23/2005 | Julia Hurwitz | SJ-02-0015A | 6654 |

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| EXAMINER | |
|---|---|
| CHEN, STACY BROWN | |
| **ART UNIT** | **PAPER NUMBER** |
| 1648 | |

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**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/540,367 | HURWITZ ET AL. | |
| | Examiner | Art Unit | |
| | Stacy B. Chen | 1648 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *23 June 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *6-16* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *6-16* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *6/23/05*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

## DETAILED ACTION

1. Applicant's preliminary amendment filed June 23, 2005 is acknowledged and entered. Claims 6-16 are pending and under examination.

### *Specification*

2. The specification is objected to because the first paragraph on page 1 should include a reference to PCT/US04/00635. Alternatively, Applicant may reference the PCT in an application data sheet in lieu of amending the specification.

### *Claims Summary*

3. The claims are drawn to a method for protecting a human subject against systemic human parainfluenza virus (HPIV) infection comprising administering a composition comprising a Sendai virus and a pharmaceutically acceptable carrier. The specification defines Sendai virus as a mouse parainfluenza virus which is the murine homologue of HPIV-1, see paragraph [0009] of the specification. The composition is administered to the upper respiratory tract of the human subject, and is in the form of a spray, one or more droplets, or an aerosol. Routes of administration include intranasal, intravenous, intramuscular, subcutaneous, intradermal, and applications to the mucosal membranes. The composition induces an HPIV-1 specific immune response, specifically, B cells, T cells (including $CD4^+$ and/or $CD8^+$), or a combination thereof. The human is less than 10 years old, less than 5 years old, or less than 1 year old. The amount of Sendai virus composition administered is between $1x10^5$ to $1x10^8$ plaque forming units (pfu). Also claimed is a method for enhancing the immune response of a subject previously infected

with HPIV to a subsequence HPIV infection comprising administering a composition comprising a Sendai virus and a pharmaceutically acceptable carrier.

### *Claim Objections*

4. Claims 11-13 are objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. Claim 11 indicates that the subject is a human, however, this limitation is already present in claim 6, from which claim 11 depends. Claims 12 and 13 are included in this objection because they are dependent on an objected claim.

### *Claim Rejections - 35 USC § 112*

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 6-16 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of inducing a B-cell immune response in a human subject against HPIV-1 by administering an unmodified Sendai virus (MPIV-1), does not reasonably provide enablement for a method of protecting, enhancing immunity, or inducing a T cell immune response in a human subject against non-HPIV-1 (*e.g.*, HPIV-2, HPIV-3 or HPIV-4) by administering any sort of Sendai virus that has been modified in any way. The specification does

not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue." These factors include, but are not limited to the breadth of the claims, the nature of the invention, the state of the prior art, the level of one of ordinary skill, the level of predictability in the art, the amount of direction provided by the inventor, the existence of working examples; and the quantity of experimentation needed to make or use the invention based on the content of the disclosure.

The breadth of the claims encompasses the protection of humans against non-HPIV-1, which includes HPIV-2, HPIV-3 or HPIV-4. This is supposedly achieved by administering any sort of Sendai virus (including Sendai virus that has been altered in any way) to the human subject. Another embodiment (claim 16) encompasses the enhancement of an immune response of a subject already infected (past or present) with any non-HPIV-1, to a subsequent HPIV infection. However, the specification discloses that it is the preparation of unmodified Sendai virus that is effective for immunizing against HPIV-1 (see specification, paragraphs [0007], [0008], and [0019]).

The nature of the invention is the induction of protective immunity against HPIV-1 using a xenotropic vaccine, the mouse homologue, Sendai virus, MPIV-1. The specification teaches that the vaccine is preferably murine Sendai virus, and according to the specification, it is MPIV-1 (see paragraphs [0006] and [0009]).

The state of the prior art shows that the African green monkey is an animal model of infection with HPIV-1, though not an animal model of disease for HPIV-1. Hurwitz *et al.* (*Vaccine*, 1997, 15(5):533-540, "Hurwitz") discloses the administration of an intranasal Sendai virus composition that protected African green monkeys from infection with HPIV-1 (abstract). Monkeys were inoculated with Sendai (mouse PIV1, Enders strain) in an amount of $7.6x10^7$ EID50, and then challenged with HPIV-1 (C35 strain), see page 534, "RESULTS" section. HPIV-1 was not detectable in the experimental monkeys following challenge with HPIV-1, while the control monkeys (receiving no Sendai virus composition and exposed to HPIV-1) became infected with HPIV-1 (page 536, columns 1 and 2). It appears that no evidence of a T cell response is recorded. Hurwitz discloses that unmanipulated Sendai virus is an effective vaccine against HPIV-1 in a primate model and may constitute a practical vaccine for human use (abstract). While Hurwitz teaches that the composition of Sendai virus is effective for inducing protective immunity in monkeys against HPIV-1, it is important to note that African green monkeys do not exhibit clinical symptoms of HPIV-1, although they are capable of being infected with HPIV-1. Thus, African green monkeys are not suitable animal models for determining any sort of therapeutic capability of the Sendai virus compositions (Hurwitz, page 538, second column, last paragraph).

Skiadopoulos *et al.* (*Virology*, 2002, 297:153-160, "Skiadopoulos") discloses that MPIV-1 (Sendai virus) replicates to a level similar to HPIV-1 in the upper and lower respiratory tract of African green monkeys and chimpanzees (abstract). Skiadopoulos warns that MPIV-1 would likely require significant attenuation (or formulated as/in a vector) prior to its being given to human subjects because of the possibility of causing zoonotic disease in humans (abstract).

Slobod *et al.* (*Vaccine*, 2004, 22:3182-3186, "Slobod") discloses a Phase I dose escalation study in healthy adults using Sendai virus (MPIV-1). Slobod discloses that the composition was uniformly well-tolerated and showed evidence of immunogenicity in three of nine vaccinees despite pre-existing cross-reactivity (abstract). Slobod characterizes MPIV-1 (Sendai virus) as a naturally attenuated live virus vaccine for HPIV-1 (page 3184, first column, "Discussion" section.)

The amount of guidance and working examples provided in the specification is similar to that disclosed in the Hurwitz reference.

Given the breadth of the claims (encompassing any type of Sendai virus formulation, effective for any type of HPIV), the nature of the invention (xenotropic vaccine), the state of the art (effective in African green monkeys, demonstrated as safe in healthy adults although young children are the susceptible subjects generally), the guidance and working examples in the specification, the specification is not enabling for the full scope of the invention as claimed. Further, although the level of skill in the art is high (evidenced by those cited in the literature, and Applicant's own work) the level of predictability in the art is low, given that the effects of this xenotropic composition on human infection/disease with regard to HPIV-1 are unknown. The Office considers the following embodiment to be enabled: A method of inducing a B-cell immune response in a human subject against HPIV-1, comprising administering an effective amount of a composition comprising unmodified Sendai virus (MPIV-1) and a pharmaceutically acceptable carrier via intranasal administration.

***Claim Rejections - 35 USC § 102***

6. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 6-10 and 15 are rejected under 35 U.S.C. 102(b) as being anticipated by Hurwitz *et al.* (*Vaccine*, 1997, 15(5):533-540, "Hurwitz"). The claims are summarized above. Note that this rejection is made with respect to the enabled aspect of the claims, not the entire scope which encompasses non-enabled embodiments (see rejection under 35 U.S.C. 112, first paragraph).

Hurwitz discloses the administration of an intranasal Sendai virus composition that protected African green monkeys from infection with HPIV-1 (abstract). Monkeys were inoculated with Sendai (mouse PIV1, Enders strain) in an amount of $7.6x10^7$ EID50, and then challenged with HPIV-1 (C35 strain), see page 534, "RESULTS" section. HPIV-1 was not detectable in the experimental monkeys following challenge with HPIV-1, while the control monkeys (receiving no Sendai virus composition and exposed to HPIV-1) became infected with HPIV-1 (page 536, columns 1 and 2). Hurwitz discloses that unmanipulated Sendai virus is an effective vaccine against HPIV-1 in a primate model and may constitute a practical vaccine for human use (abstract). Therefore, the embodiments of claims 6-10 and 15 are anticipated by the prior art.

***Claim Rejections - 35 USC § 103***

7. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 12-14 are rejected under 35 U.S.C. 103(a) as being obvious over Hurwitz *et al.* (*Vaccine*, 1997, 15(5):533-540, "Hurwitz"). The claims are summarized above, as are the teachings of Hurwitz. Note that this rejection is made with respect to the enabled aspect of the claims, not the entire scope which encompasses non-enabled embodiments (see rejection under 35 U.S.C. 112, first paragraph).

Although Hurwitz does not name the specific ages of the young children that are affected by HPIV-1 infection and disease (Hurwitz, abstract, first sentence, and page 533, column 1, first sentence), it would have been obvious to administer Hurwitz's composition to children that are under the age of 10, 5 and less than a year old, since HPIV-1 is known to infect and cause disease in children, even infants that have "croup" (Hurwitz, page 533, column 1, first sentence). Given what is known regarding the patient population of HPIV-1, it would have been obvious to administering Hurwitz's composition to children under 10 years old with a reasonable degree of predictability.

***Conclusion***

8. No claim is allowed. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Stacy B. Chen whose telephone number is 571-272-0896. The examiner can normally be reached on M-F (7:00-4:30). If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Bruce Campell can be reached on 571-272-0974. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

/Stacy B. Chen/ 8-30-2007
Primary Examiner, TC1600